



# Management of acute ischemic stroke after pulmonary resection: incidence and efficacy of endovascular thrombus aspiration

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## Abstract

**Objective** We analyzed acute ischemic stroke by thromboembolism in the early period after lung cancer surgery.

**Methods** A retrospective review of the clinical records of patients who underwent lung resection for primary lung cancer was performed. Patients who underwent lobectomy, bilobectomy, and pneumonectomy were included. The clinical characteristics of the patients, the incidence of atrial fibrillation (Af) after surgery, and the incidence of acute ischemic stroke were analyzed. The clinical courses of patients having acute ischemic stroke were also reviewed.

**Results** In 4 (0.6%) of 696 patients, acute ischemic stroke occurred in the early period during hospitalization after lung cancer surgery. Acute ischemic stroke occurred within 4 days in three cases and after 4 days in one case. The resection site of the lung was the left side in all cases, and there were three cases of left upper lobectomy and one case of left lower lobectomy. As for the two recent patients, thrombus removal was performed by a neurosurgeon, and both cases achieved successful recanalization. The time between symptom detection and recanalization was 205 and 170 min, respectively. One patient was cured without any residual effect of disease, and the other patient's hemiplegia resolved and aphasia improved.

**Conclusion** Since cerebral infarction impairs the patient's quality of life, thrombus removal should be considered if possible.

**Keywords** Thrombus removal · Acute ischemic stroke · Cerebral infarction · Lung cancer surgery

## Introduction

Perioperative acute ischemic stroke (AIS) after pulmonary lobectomy/pneumonectomy is uncommon. However, permanent neurological disability following AIS presents a formidable burden to patients, their families, and communities.

The causes of AIS after lung resection are multifactorial, such as thromboembolism from the stump of the pulmonary vein [1] or from the left atrium in atrial fibrillation (Af), paradoxical embolism from deep venous thrombosis, or acute thrombotic occlusion of the intracranial arteries in elderly patients. Of these, the most common culprit is Af

during the early postoperative period. Hypercoagulability after major surgery may trigger formation of thrombus, with tumor-induced thrombosis.

In this report, the clinical records of patients who developed AIS after lung resection were reviewed, and a new team approach for patients with this clinical entity is proposed.

## Patients and methods

A retrospective review of the clinical records of patients who underwent lung resection for primary lung cancer in Hirosaki University Hospital was performed.

The study period was January 2005 to December 2016. Patients who underwent lobectomy, bilobectomy, and pneumonectomy were included. Patients who underwent segmentectomy and partial resection of the lung for primary/metastatic lung cancer were excluded. The clinical characteristics of the patients, the incidence of Af after surgery, and the incidence of AIS were analyzed. The clinical courses of the AIS patients were also reviewed.

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## Surgical technique

All patients underwent the standard procedure for anatomical pulmonary resection, with division of the pulmonary veins using an automated sutured device or surgical ligation under videoscopic monitoring. Systematic lymph node dissection was performed to achieve curative resection.

## Definition and diagnosis of AIS

AIS was suspected based on the appearance of a new neurological deficit including major motor weakness, speech disturbance, and somnolence. Emergent computed tomography (CT) of the brain was performed to exclude hemorrhagic stroke. Then, brain magnetic resonance (MR) angiography was performed to show occluded arteries. In the two recent cases, neurosurgeons were immediately consulted to decide on the indication for diffusion-weighted magnetic resonance imaging of the brain and early reperfusion by endovascular thrombus aspiration.

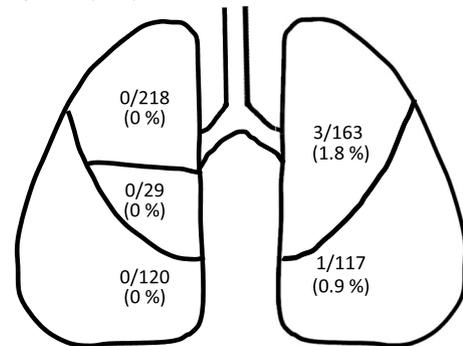
## Results

The total number of pulmonary procedures including lobectomy, bilobectomy, and pneumonectomy was 696, with 647 lobectomies, 34 bilobectomies, and 15 pneumonectomies. The laterality of surgery was right side in 403 and left side in 293. There were 432 male and 264 female patients.

Of the 696 cases, 4 (3 male, 1 female) developed AIS after lobectomy for lung cancer. The incidence of AIS was 0.6% (Fig. 1). All four patients had left-sided surgery. The patients' ages ranged from 58 to 76 years (average 68.0 years) (Table 1). The onset of cerebral infarction was on postoperative days 2–9. Operation time was 180–439 min, and blood loss was 20–500 g; three patients underwent left upper lobectomy, and one patient underwent left lower lobectomy. The pulmonary vein was divided by stapler in three patients, and it was ligated in one patient. While two patients had postoperative atrial fibrillation (Af), the other two patients did not have Af. Twenty-six patients had postoperative Af (14 patients after left lobectomy and 12 patients after right lobectomy). The prevalence of stroke among those who had postoperative Af was 7.7%, while the prevalence of stroke among those who did not have Af was 0.3% (Table 2).

The occluded arteries were the right middle cerebral artery in three patients and the left middle cerebral artery in one patient (Table 1). The two early cases were treated conservatively, while the two most recent cases underwent thrombus removal by a neurosurgeon, and both achieved

### I. single lobectomy 4/677 (0.6%)



### II. bilobectomy 0/34 (0%)

rt. upper-middle lobectomy 0/17 (0%)  
rt. middle-lower lobectomy 0/17 (0%)

### III. pneumonectomy 0/15 (0%)

rt. Pneumonectomy 0/2 (0%)  
lt. pneumonectomy 0/13 (0%)

**Fig. 1** Incidence of acute ischemic stroke after pulmonary resection. ( ) indicates rate of AIS

successful recanalization. In case 3 and case 4, the time between symptom detection and recanalization was 205 and 170 min, respectively. While one patient (case 3) recovered without any residual effects, in case 4 (Figs. 2, 3) hemiplegia resolved, but mild aphasia remained at discharge.

Chest CT scan or echocardiography was not performed in case 1 after AIS. In other three cases, enhanced chest CT scan were performed after the onset of AIS. There was no thrombus in the pulmonary vein stumps. Echocardiography was also performed in cases 2, 3 and 4. In case 2, thrombus was detected in the left atrium by echocardiography. In cases 3 and 4, thrombus was not detected in the left atriums. In case 4, interatrial septal aneurysm was detected by echocardiography.

## Discussion

The incidence of AIS after lung surgery is as low as 0.6% in the United States [2] and 0.3% in Japan [3]. In the present series, three of four patients had left upper lobectomy, and only one had left lower lobectomy. Two of four patients had transient Af at the onset of AIS. Af in the perioperative period is regarded as a major cause of AIS, not only in lung surgery, but also in the general population. The prevalence of Af increases proportionally with age, and aging is an important predictor of AIS in the general population [4]. In the present study, 26 cases had postoperative Af. The prevalence of postoperative Af is as high as 3.7% and among them, two cases developed AIS postoperatively. In case 3, the upper pulmonary vein was divided in the pericardium due to tumor invasion of pulmonary vein; therefore, the stump of the pulmonary vein was very short. AIS occurred when the heart rhythm returned to sinus rhythm after transient Af.

**Table 1** Summary of acute phase cerebral infarction patients with removal of thrombus after pulmonary lobectomy

Cases	Age	Sex	Preoperative complication	Location of lobectomy	Resected organs	Pulmonary stump treatment	Operation time (min)	Blood loss (g)	Postoperative period	Initial symptoms and sign	Thromboembolism location of	Pathological stage/histological type	Postoperative af	Neurological outcome at discharge
1	71	M	COPD, ASO	Left upper	None	Ligation	193	114	9	Hemiplegia, somnolence	Right middle cerebral artery	IA/adenocarcinoma	No	No recovery
2	58	M	Gastric ulcer	Left upper	None	Stapler	251	98	4	Dysarthria, aphasia	Right middle cerebral artery	IA/adenocarcinoma	Yes	No recovery
3	76	M	Prostatic hypertrophy	Left upper	Pericardium, phrenic nerve	Stapler	439	500	2	Facial nerve palsy, hemiplegia	Right middle cerebral artery	IIIA/adenocarcinoma	Yes	Full recovery
4	67	F	Hypertension, uterine fibroid	Left lower	None	Stapler	180	20	4	Aphasia, somnolence	Left middle cerebral artery	IB/adenocarcinoma	No	Remaining of mild aphasia

*COPD* chronic obstructive pulmonary disease, *ASO* arteriosclerosis obliterans

**Table 2** Incidence of stroke under Af

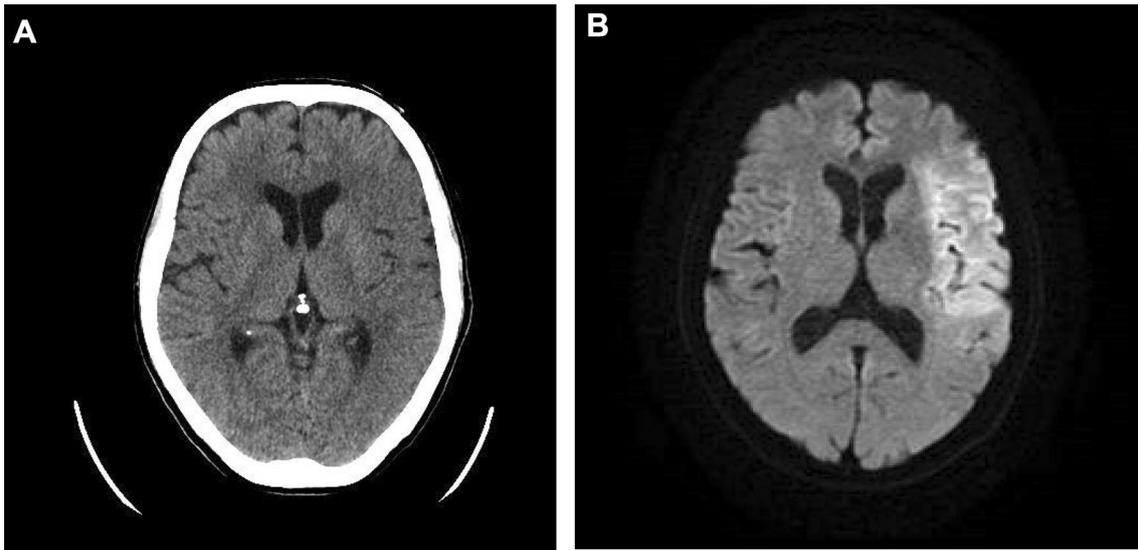
	Total	Stroke	Incidence (%)	[95% CI]
Af (–)	647	2	0.3	[0.26–0.34]
preoperative Af (+)	23	0	0	
postoperative Af (+)	26	2	7.7	[0.06–0.10]

Grimm et al. theorized that worsening left atrial appendage function occurs after spontaneous conversion from atrial fibrillation/flutter to sinus rhythm. It causes thrombogenesis in the left atrium and thromboembolism [5]. In our case, such a mechanism might have acted. Xin et al. reported that the patients who underwent a left lobectomy had a higher incidence of postoperative Af than those who underwent a right lobectomy. They also pointed out that B-type natriuretic peptide (BNP) was a predictor of postoperative Af in patients who underwent a left lobectomy [6]. However, Ueda et al. reported there was no significant difference in the incidence of postoperative Af between the resected sites [7]. In our series, incidence of Af was high but it was statistically not different between left and right lobectomy group, because of volume of study population was small. Two patients did not show signs and symptoms of atrial arrhythmia at onset. No episode of Af was observed during the perioperative period in case 4.

Virchow’s triad is very important for the generation of thrombus [8]. Postoperative Af is a major risk factor for AIS in patients undergoing coronary artery bypass grafting [9]. In case of atrial fibrillation, stasis of blood flow in the left atrium causes clot formation combined with postoperative inflammatory reaction. Ohtaka et al. reported that turbulence is made within the long pulmonary vein stump [1].

Yamamoto et al. reported a high frequency of cerebral infarction in patients who underwent left upper lobectomy for lung cancer [10]. Ohtaka et al. assumed that, since the stump of the left upper pulmonary vein is longer than other stumps for anatomical reasons, stagnation of blood flow may cause thrombus formation in the stump [1]. In case 4, interatrial septal aneurysm might evoke turbulence and form thrombus. Pearson et al. reported atrial septal aneurysm was an independent risk factor of AIS [11]. Therefore, on the AIS cases after lung cancer surgery it might be important to perform chest CT scan and echocardiography to search PV stump thrombosis, thrombus in the left atrial appendage, atrial septal aneurysm, and patent foramen ovale. In patients having patent foramen ovale, screening for venous thromboembolism is also necessary to exclude paradoxical embolism.

A revolutionary change in AIS management has been occurring over this decade. Systemic administration of recombinant tissue plasminogen activator (rt-PA) was shown to be useful to obtain recanalization of occluded cerebral



**Fig. 2** Brain CT (a) and MRI (magnetic resonance imaging) (b) of case 4. **a** The cortico-medullary junction was unclear in the left frontal lobe and island. The cerebral sulcus was narrow on the head CT

scan (early CT sign). **b** Diffusion-weighted imaging showing subtle ischemic changes in the territory of the left middle cerebral artery



**Fig. 3** Angiography of the internal carotid artery of case 4. The left middle cerebral artery was occlusive before operation. After thrombectomy by penumbra system, angiography show complete reperfusion of the left middle cerebral artery

arteries. However, hemorrhagic complications, such as transformation of hemorrhagic infarction and wound bleeding, are major adverse events. Therefore, administration of rt-PA is contraindicated after major surgery due to concern about critical wound hemorrhage [12]. The advent of endovascular aspiration of thrombus resulted in a drastic change in AIS management. The Penumbra Aspiration System (Penumbra, Alameda, CA, USA) was introduced for clinical use in 2011, with reimbursement by the insurance system. In the Penumbra Pivotal Stroke Trial, 125 patients with AIS due to occlusion of large cerebral vessels were enrolled. The recanalization rate was as high as 81.6% in the treated vessels, with a low incidence of adverse effects [13], and neurological improvement was significantly better than in the control group. Ikeda et al. first reported thrombus removal after lung cancer surgery [14]. Only four cases treated by thrombus removal for cerebral infarction after lung cancer surgery have been reported in the literature (Table 3). Three cases occurred after left-side lobectomy, and only one case occurred after right-side lobectomy. Thrombus was removed successfully in all cases [14, 15].

We consider that thrombus aspiration is efficacious for AIS after lobectomy. In the two recent cases presented, aspiration of cerebral thrombus was successful, and there was no residual stenosis in the cerebral arteries, indicating embolism as the cause of AIS. The technical success rate was 100%, including two of the present cases, and neurological outcomes were also satisfactory.

### Conclusions

Embolic stroke occurred after pulmonary surgery in 0.6% of cases, with an incidence of 1.8% after left upper lobectomy. Thrombus aspiration therapy is a promising strategy for AIS after lung surgery to improve neurological outcomes. A team approach for early recognition of stroke, diagnostic evaluation with MRI, and early revascularization is the key to improving neurological outcomes.

### Compliance with ethical standards

**Conflict of interest** The author has declared that no conflict of interest exists.

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**Table 3** Summary of patients with cerebral infarction within sebral days after pulmonary lobectomy

Year	Authors	Age	Sex	Location of lobectomy	Post-operative period	Location of embolism	Symptoms	Suspected cause of embolism	Artery of embolism	Results
2014	Ikeda [7]	58	M	Left upper	2 days	Brain, spleen	Consciousness disorder, hemiplegia, aphasia	Thrombus formation in pulmonary vein stump	Internal carotid artery	Successful
2014	Tanaka [8]	70	M	Right upper	12 days	Brain	Consciousness disorder, hemiplegia	Unknown	lt. middle cerebral artery	Successful
2016	Present case 3	76	M	Left upper	2 days	Brain	Hemiplegia, facial nerve palsy	af	rt. middle cerebral artery	Successful
2016	Present case 4	67	F	Left lower	4 days	Brain	Hemiplegia, aphasia, somnolence	Unknown	lt. middle cerebral artery	Successful

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